

identifying a first nucleic acid sequence in the subpopulation of nucleic acid sequences;  
and

comparing the first nucleic acid sequence to a reference nucleic acid sequence or sequences, wherein the absence of the first nucleic acid sequence in the reference nucleic acid or nucleic acid sequences indicates the first nucleic acid is a novel nucleic acid sequence.

Sub C6  
(20) (Amended) A method for equalizing the representation of nucleic acids in a population of nucleic acids, the method comprising in order the steps of:

providing a population of cDNA molecules derived from a population of RNA molecules, wherein said population comprises a first nucleic acid and a second nucleic acid having a nucleic acid sequence distinct from the first nucleic acid, and wherein said first nucleic acid is present at a higher level in said population than said second population;

partitioning said population into one or more subpopulations of nucleic acids, wherein said partitioning comprises digesting the cDNA molecules with one or more restriction enzymes;  
and

lowering the level of said first nucleic acid sequence relative to the level of said second nucleic acid sequence in the subpopulation of nucleic acid sequences, thereby equalizing the representation of nucleic acids in said population of nucleic acids.

Add the following new claims:

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Sub C7  
--27. The method of claim 1, wherein the partitioning comprises one or more processes chosen from the group consisting of a) isolating nucleic acids from different cell types, b)

separating the nucleic acids in the subpopulation by size, c) amplification that provides a subpopulation of nucleic acids, d) preferentially amplifying 5' terminal sequences of the nucleic acids, e) preferentially amplifying interior sequences of the nucleic acids, and f) preferentially amplifying 3' terminal sequences of the nucleic acids.

Sub C7

28. A method of identifying a novel nucleic acid sequence, the method comprising:

- providing a population of nucleic acid molecules;
- normalizing the population to provide one or more subpopulations of nucleic acids;
- determining the sequence of a plurality of nucleic acid molecules in the one or more subpopulations;
- assembling a plurality of nucleic acid sequences to provide an assembled sequence; and
- determining whether the assembled sequence is absent in a reference set of one or more reference nucleic acid sequences;

whereby if the absence of the assembled sequence from the reference indicates the assembled sequence is a novel nucleic acid sequence.

Revised

29. The method of claim 28, wherein the normalizing comprises partitioning.

Sub C8

30. The method of claim 29, wherein the partitioning comprises one or more processes chosen from the group consisting of a) isolating nucleic acids from different cell types, b) separating the nucleic acids in the subpopulation by size, c) amplification that provides a subpopulation of nucleic acids, d) preferentially amplifying 5' terminal sequences of the nucleic acids, e) preferentially amplifying interior sequences of the nucleic acids, f) preferentially

Sub C8 amplifying 3' terminal sequences of the nucleic acids, and g) hybridization of said population against a prepared library of known nucleotide sequences.

31. A method of screening a population of nucleic acids for a novel sequence, the method comprising:

providing a population of cDNA molecules derived from a population of RNA molecules;

partitioning said population into one or more subpopulations of nucleic acids, wherein said partitioning comprises digesting the cDNA molecules with one or more restriction enzymes;

identifying a first nucleic acid sequence in the subpopulation of nucleic acid sequences;

and

comparing the first nucleic acid sequence to a reference nucleic acid sequence or sequences, wherein the absence of the first nucleic acid sequence in the reference nucleic acid or nucleic acid sequences indicates the first nucleic acid is a novel nucleic acid sequence.

Sub C9 32. A method of screening a population of nucleic acids for a novel sequence, the method comprising:

providing a population of nucleic acid sequences;

normalizing said population into one or more subpopulations of nucleic acids, wherein said normalizing is selected from the group consisting of restriction endonuclease digestion, size-based fragment partitioning; terminal nucleotide sequence, and fragment migratory pattern;

identifying a first nucleic acid sequence in the subpopulation of nucleic acid sequences;

and